HEREDITARY SYPHILIS IN THE LIGHT OF RECENT CLINICAL STUDIES.[1]

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Transmission. Whatever may have been the real position of Paracelsus—whether a great physician out of touch with his times or a master quack—we must credit him with being the first to assert the existence of an inherited form of syphilis. This was in the year 1529, a short time after the introduction of the disease into Europe from the West Indies; but a general belief in the transmission of syphilis from parents to offspring did not prevail until the latter part of the seventeenth and eighteenth centuries, although an infantile form of syphilis was well recognized. With the acceptance of the general idea there has been a century-long controversy in regard to the details of the method of transmission, which, expressed in its simplest form, has centered about the question of whether or not syphilis in the father can be transmitted to the child *in utero* without the mother at the same time becoming infected.

Without going into the historical details of the years of controversy, we can briefly sum up the position taken by the two most prominent groups of syphilographers. One group has held to the view of germinal transmission, which to a large extent is based upon the observations that:

1. In most cases of inherited syphilis the father is admittedly syphilitic.
2. That many women without clinical signs or history of lues bear syphilitic children to a syphilitic father.
3. That the treatment of a syphilitic father in many instances has lead to the mother bearing normal children after having previously given birth to a syphilitic child.
4. That instances are known of where an untreated woman has borne syphilitic children to a syphilitic father and subsequently normal children to a normal father.

The last two observations do not always hold true and the question at issue really involves the second observation—that is, of healthy mothers giving birth to syphilitic children. It is admitted that in many cases the mother is syphilitic, being anteconceptionally, conceptionally, or postconceptionally infected.

In 1837 Colles published the observation that apparently normal women bearing syphilitic children acquire an immunity to syphilis, or, more correctly, do not contract syphilis when exposed to infection. This has been interpreted in two ways: (1) as an expression of a passive immunity due to the absorption of immune bodies from the syphilitic fetus through the placenta, and (2) as the result of an active immunity, the woman having syphilis. According to the ideas of those who believe that in all cases the mother is infected, it is only the negative Colles' mothers—that is, the few reported cases in which the mothers of syphilitic children have subsequently become infected with syphilis—which lend any valid support to the theory of the possibility of a purely paternal infection, and the accuracy and correctness of the clinical observation has been questioned in these cases. The second group, as we have said in discussing the first, holds to the view that the mother is always infected, and that without maternal syphilis there is no syphilis of the offspring.

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[1] Read before the Kansas City Academy of Medicine, January 7, 1916.

This controversy, which lasted for so many years, was based upon the interpretation of clinical observation, and in brief depends upon whether or not germinal infection is possible—that is, whether the spermatozoön can carry the infection and the offspring become syphilitic without the mother acquiring the disease. Within the last decade—for it was in 1906 that Schaudinn's first paper appeared—our knowledge of syphilis has increased more than in the entire period of time elapsing since its recognition in the latter part of the fifteenth century, and the discovery of the etiological organism and of serodiagnostic methods have helped to clarify in many ways the questions which have confused this subject of inherited transmission.

The Treponema pallida of Schaudinn is an organism some 6 to 15 microns in length and with some 10 to 26 undulations. The head of a spermatozoön—which is the only portion capable of carrying an organism within it—is from 3 to 5 microns in length. Hence, the physical impossibility of the treponema being carried in the spermatozoön, which is essential if we are to have a true germinal transmission, unless the organism undergoes some morphological change in its life history with which we are at present unfamiliar and have no reason to suspect. Moreover, we know of no example of germ-cell transmission of an infectious disease in human or veterinary pathology. With everything thus against the possibility of such a method of transmission the burden of proof is with those who advance the theory, and as yet no evidence has been submitted in support of their position.

Although, in all probability, germinal transmission does not occur, as we have seen, it has been found that the seminal fluid can carry the infection, and the testicles are recognized as a not infrequent seat of latent syphilis. Finger was able to transmit an infection to two of the higher apes with seminal fluid from florid lues, and Neisser has transmitted the infection by transplanting the testicles of syphilitic apes. It has not been possible to demonstrate the presence of spirochetes in seminal fluid by microscopic methods. These experiments, it must be kept in mind, only prove the infectiousness of seminal fluid from active syphilitics, and do not bear a direct relation to the question of paternal transmission in hereditary syphilis.

Turning now to the question of women bearing syphilitic children who show no signs of syphilis: There are two possibilities—either the women are not syphilitic, or else they have syphilis in an inactive or latent form. With the development of serological methods for the diagnosis of syphilis, their applicability to this question was at once recognized and many small series of tests were soon reported. In these small series the percentage of positive reactions in the blood of mothers of syphilitic children ran from 40 to 60.

In a recent study of familial syphilis made in our clinic in St. Louis we had occasion to test the blood of 85 mothers of syphilitic children. Of these 85 mothers, 74, or 87 per cent., denied all knowledge of infection, nor was there anything in the history given us that would indicate a syphilitic infection outside of a history of frequent abortions. Dr. Jeans[2] has recently collected these cases and found that the blood of 73 of the 85 gave a positive Wassermann test. Of the remaining 6 all but one were tested after an interval of at least ten years had elapsed between the birth of the last syphilitic child and the time of the test. In the one exception the interval had been four years. In some of these cases a healthy child had been born during this period.

In this way, by means of the complement-deviation test, it has been found presumable that these apparently healthy mothers are immune, in Colles' sense, because they have syphilis in a latent form. Hochsinger, in order to uphold his older ideas, would have us believe that in these cases the positive reaction was an indication of immunity rather than of infection. This interpretation is incorrect, as a positive Wassermann indicates tissue response against superinfection due to the presence of the spirochetes rather than a true reaction of immunity. As long as the reaction remains positive a superinfection never occurs, but it is well known that when treatment has been pushed to a point where it has become persistently negative, a second "primary" infection has occurred in many cases. Thus we do not have an immunity in syphilis in the true sense of the term, and a positive Wassermann signifies infection. Hence, we must regard it as evidence of or a symptom of syphilis whether the infection is active or latent, as in the cases under discussion.

In the present state of our knowledge we can summarize the evidence as pointing to the view that in hereditary syphilis the mother is always infected, although very frequently the infection is latent and that true germinal infection does not occur.

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[2] Familial Syphilis, Am. Jour. Dis. Child., 1916, xi, 11.

SYPHILIS AS A SOCIAL PROBLEM. No accurate figures are available as to the incidence of hereditary syphilis. The disease is not reportable, and even if it were it is doubtful if the records obtained in this way would be of any value, as the condition is frequently overlooked, and when recognized would be concealed in many cases because of the stigmata attached. With improved methods of diagnosis we are beginning to learn that it is far more common than previously thought, as many conditions in which the etiology was obscure have been found to be the result of a syphilitic infection. Hospital statistics are of little value in this connection. In St. Louis we have been particularly interested in hereditary syphilis, and have admitted many cases to the Children's Hospital for study which would normally have been cared for in the out-patient clinic, and hence the proportion of syphilis to the total number of admissions is relatively high. We have seen between 300 and 350 children with an hereditary infection in three and a half years and have undoubtedly failed to recognize a number of cases. We have also found many cases of latent syphilis by testing the apparently healthy children of syphilitic families. What is more important is the number of obscure clinical conditions which have been found to be syphilitic in origin.

The importance and cost of syphilis to the family and the community is not generally appreciated. About this point we have collected some interesting information: For a period of about a year an attempt was made to obtain extensive data in regard to the family of every syphilitic child coming to the clinic, to examine all of the other living children as well as the parents, and to test the blood of each member by the complement-deviation method. In this way data was assembled for 100 syphilitic families. Many marriages (10 to 30 per cent.) remain sterile as a result of syphilis and others (13 per cent. according to Haskell) result only in abortions. Our material includes only those families in which a living child came under our direct observation and care.

In these 100 syphilitic families 331 pregnancies occurred which resulted as follows:

Abortions	100 or 30.2	per cent.
Stillbirths	31 or 9.3	"
Living births	200 or 60.5	"

Thus 40 per cent. of the pregnancies terminated in the death of the fetus before term. If the parents had been healthy and of the same social strata we might have expected 30 to 35 deaths before term, or a mortality of 10 per cent. instead of 40 per cent.

Considering next the 200 living births: At the time the data were collected 39 were dead and 161 alive, but 12 of the 161 died during the course of the investigation. Of the 161 examined 107 had both clinical signs of syphilis and a positive Wassermann; 5 were clinically positive but gave negative tests (in all of these the family gave a history of syphilis); 16, although negative as regards clinical manifestations, gave positive reactions, and therefore belong to the group of latent syphilitics. Thus but 33 of the 161 living children were free from the infection, and if we attribute the deaths occurring before term to syphilis, we find that of the 331 pregnancies in 100 syphilitic families but 10 per cent. escaped the infection. The toll is summarized in the following table:

331 PREGNANCIES IN 100 SYPHILITIC FAMILIES.

131 or 40 per cent. died before term	55 per cent. dead
51 or 15 per cent. died after birth	
116 or 35 per cent. living but syphilitic	35 per cent. syphilitic
33 or 10 per cent. living and free from syphilis	10 per cent. escaped
331	

If we add to this record and take into consideration the physical condition of the parents—both of whom were syphilitic in almost all of our cases—we begin to grasp the appalling importance of syphilis from a social standpoint.

In order to show this in another way, studies[3] were made in our clinic in which the waste (total deaths to total pregnancies) occurring in 100 families in which we were treating children with contagious disease, and in 100 families selected at random from our records, were contrasted with the waste in 100 syphilitic families. These groups are designated as C. R. and S. respectively and the data briefly summarized in the following table:

Group.	Total pregnancies.	Deaths before birth.	Born living now dead.	Total.	Per cent. waste.
C.	444	46	70	116	26
R.	442	42	59	101	22
S.	453	116	104	220	48

The increase in the waste for the syphilitic group of 100 per cent. does not represent the total waste, as it is fair to assume that three-quarters of the living children are syphilitic and many of these defective.

There are many things of interest in connection with the question of family syphilis—the way in which the infection seems to die out, the apparent tendency to involvement of the nervous system in some families, for example, which cannot be discussed in the limits of this paper. The question of the transmission to the third generation, about which so much has been written by Fournier, requires mention in passing. In the light of recent discoveries this entire chapter must be rewritten, as definite tests can now be applied when before we had to rely upon clinical observation which was questionable in many of the cases quoted as examples of this form of transmission. Today, in order to prove existence of an infection being transmitted to the third generation, we must not only have a positive Wassermann test in the child, its mother, and its maternal grandmother, but also in the brothers and sisters of the mother. This is essential to exclude faulty observation, and cases fulfilling these conditions must be adduced before we can state definitely that transmission to a third generation occurs. We have no cases fulfilling these conditions in our records, although in some cases there is a strong clinical suggestion of such a mode of transmission. We recently had in the hospital the child of a mother with inherited syphilis. The child was mentally and physically defective, but was free from a true specific infection. This is probably the form in which hereditary syphilis shows itself most frequently in the third generation, but these children are not syphilitic in the sense of true inherited transmission.

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[3] Jeans and Butler, Hereditary Syphilis as a Social Problem, Am. Jour. Dis. Child., 1914, viii, 327.

CLINICAL MANIFESTATIONS. Passing now to a consideration of some points in regard to the clinical manifestations of hereditary syphilis.

From a clinical standpoint we have found it of service to divide our cases of inherited syphilis into four groups:

1. Fetal.
2. Infantile.
3. Late or tardy.
4. Latent.

In the first group, under the term fetal syphilis, we include the cases in which manifest signs of lues develop *in utero*. Thus, stillborn as well as living infants are included. It is this form of syphilis which the obstetrician sees in his practice and the death rate is extremely high for the infants born alive. In the second group, infantile hereditary syphilis, are placed the cases which develop clinical lesions after birth and during the first year of life, and in the third group, "late" syphilis, those cases developing symptoms after the first year regardless of whether or not there have been previous symptoms during infancy. The last (fourth) group is made up of apparently normal children whose blood gives a positive Wassermann reaction. This group, as a rule, goes unrecognized unless some other member of the family shows clinical signs of syphilis and thus furnishes a reason for a blood test being made. That these cases are not uncommon is shown by the number of children developing "tardy" lesions with a negative history as regards clinical manifestations during infancy. While the "infantile" lesions have doubtlessly been overlooked in some of these patients with "late" lesions, this can hardly be the case with all. In the series reported above there were 16 latent cases among the 116 living syphilitic children in the 100 families.

One of the most striking things about the clinical manifestations of hereditary syphilis is the distinctive and almost uniform character which the lesions show in the infantile group and the varied and bizarre ways in which the syphilitic infection appears in the late cases. This has been compared with the secondary and tertiary manifestations of acquired syphilis, and in general the comparison is good, although not strictly accurate. There is no distinctive primary lesion in inherited syphilis in the sense the term is used in the acquired form, as the infection takes place through the blood. As will be shown below there is a certain period of latency or incubation time between the time the infection takes place *in utero* and the development of visible symptoms after birth, which in a way corresponds to the time elapsing between the appearance of the chancre and the secondary lesions in acquired syphilis. There is no satisfactory explanation of why syphilis develops in such diverse ways. It would seem probable that whether fetal or infantile syphilis develops in a given case depends upon the time infection takes place *in utero*, infection early in pregnancy leading to early death and abortion, and infection occurring late to the infantile cases. Between these two may be innumerable gradations.

As the infantile and tardy groups are the most important I wish to discuss these in more detail. I have recently, together with Dr. Jeans,[4] studied the records of 100 consecutive cases of the infantile type, and, unless otherwise stated, the figures given below refer to this series. Where the totals are under 100 for any given point it means that the data regarding the point under consideration were unsatisfactory in the number of cases omitted.

As a rule, the first clinical symptoms of the infantile group develop in the first two months of life (81 per cent.), and the majority of these in the first month. In the accompanying table the time of development of the earliest symptom is shown for 95 cases:

Time of appearance.	Cutaneous eruptions.	Rhinitis.	Epiphysitis.	Wasting and Wassermann.	Jaundice.	Hemorrhage and edema.	Total.	
1 week . .	4	12	..	..	..	.....	10	Total in first month, 51
2 weeks . .	2	3	..	..	..	.....	5	
3 weeks . .	3	6	5	..	..	.....	14	
4 weeks . .	7	6	2	..	..	1	16	
5 weeks . .	..	1	1	..	..	.....	2	Total in second month, 30
6 weeks . .	6	7	..	..	..	.....	13	
7 weeks . .	2	3	..	..	..	.....	5	
8 weeks . .	6	1	1	1	1	.....	10	
3 months .	5	1	..	..	..	.....	6	
4 months .	1	1	..	3	..	Iritis 1	6	
6 months .	1	..	..	..	..	.....	1	
10 months .	1	..	..	..	..	.....	1	
Total .	38	41	9	4	1	2	95	

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[4] Observations on Infantile Syphilis, Am. Jour. Dis. Child., 1916, xi, 177.

In the majority of the infants developing lesions early a rhinitis or coryza was first noted, but in the entire group the number of cases in which a rash was noted first is about the same. The most striking thing about these cases is that so many do not develop lesions until so long after birth, although infection takes place *in utero.* Two explanations are possible: one is that the infection varies both quantitatively and qualitatively in different cases—that is in one few organisms and in another many may gain entrance—or that the organisms may vary considerably in their virulence. With these variables any number of gradations are possible. A very plausible explanation, suggested by Rietschel, is that in these infantile cases the fetus is not infected until near the end of the pregnancy, when the beginning uterine contractions, which may precede parturition by a number of days, open a portal of entrance for infection by breaking loose the placental villæ and tearing open the sinuses, in this way opening a direct route for the transmission of the spirochetes. After a more or less definite period of time clinical signs of the infection appear, and the length of this time after parturition is dependent upon the time previous to parturition at which infection takes place. There are a number of obvious objections to this being more than a partial explanation.

It is a common statement that syphilis in an infant shows itself in two ways: either by producing a general dystrophic condition or by the appearance of more or less specific lesions. As a matter of fact, the two are usually combined and the first occurs but rarely as an entity. It was formerly supposed that many of the various congenital malformations had a luetic basis, but it has been shown by the Wassermann test that there is no relationship between the two more than that of a chance association. Thus, Holt[5] did not find a single syphilitic infection among 56 consecutive infants with congenital malformations (spina bifida, congenital heart disease, hare-lip, etc.), and in our experience it is not a common occurrence, although we have found the two occasionally associated. On the other hand, Browning[6] obtained 17 positive reactions in 20 patients with congenital heart disease, and Findlay,[7] of Glasgow, in 7 of 11 patients. In the parents of 2 of the 4 negatively reacting cases the reaction was positive. Naturally, I am inclined to trust our own experience and doubt very much if there is any etiological relationship between inherited syphilis and congenital malformations.

As intimated above the specific infection exerts a harmful influence upon the nutrition of the infant much greater than that which accompanies any type of chronic or acute infection, and this, no doubt, is the result of the widespread distribution of pathological lesions throughout all of the viscera. To show the extent of this malnutrition we compared the weights of 77 syphilitic infants at the time of the first examination with the average weights of a like number of normal infants of the same ages: 7 were overweight, 10 of average weight, and 60 below average weight. The entire group of 77 cases averaged 1480 gms., or a little more than 3 pounds below weight. This wasting, or malnutrition, is of extreme importance, as the outcome of any individual case depends more upon the state of the infant's nutrition than upon the specific treatment.

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[5] Wassermann Reaction in Hereditary Syphilis, etc., Am. Jour. Dis. Child., 1913, vi, 166.

[6] Syphilis and the Health of the Community, British Med. Jour., 1914, i, 77.

[7] Hereditary Syphilis, Glasgow Med. Jour., 1914, lxxxii, 401.

Associated with this wasting the large part of the cases of infantile syphilis show one or more of three symptoms: a rash, a rhinitis or coryza, and a palpable spleen. The first was present in 77 per cent., the second in 74 per cent., and the third in 82 per cent. of the 100 cases in our series. These might be called classical symptoms and require no discussion, but in passing I might add that in our series a desquamative dermatitis, particularly of the palms of the hands and the soles of the feet, was far more common than a macular or maculopapular eruption. This is contrary to the teaching in most text-books.

Epiphysitis is a common lesion and can be demonstrated in many of the stillborn infants by incision through the lower end of the femur, or by a line of enlarged calcification seen in roentgenographs of long bones in infants with syphilis. In these cases nothing is visible clinically until the process extends to the tissues surrounding the bone and the muscles become involved. This produces "Parrot's pseudoparalysis," which is erroneously termed epiphysitis. This external involvement was present in 14 of the 100 cases in our series. A condition frequently overlooked is an iritis or choroiditis in early infancy. Everyone is familiar with the keratitis of "late" syphilis, but eye examinations, and particularly ophthalmoscopic examinations, of young infants are so infrequent that these ocular manifestations which we find quite frequently are missed in many cases.

Perhaps the question of greatest interest in connection with these syphilitic infants is their outcome or future; 40 per cent. of the infants in our series died in the first year of life, and this despite the fact that most of them received intensive treatment. Other observers report a similar or higher mortality, and I have not run across any lower figures. Among those who do not die a small number develop lesions which lead to permanent symptoms—cerebrospinal syphilis, etc.—and in the sense that these permanent changes are the result of syphilis may be said never to clear up. In about half of the cases the signs of the infection disappear, either as the result of treatment or seemingly from some inherent reason. Unfortunately these cases are, as a rule, lost from view.

In a certain percentage of children developing late lesions there is a history of infantile lesions, but it would seem that in some of these early cases the infection becomes latent or dies out. There are no statistics on record of how many infantile cases develop late lesions. Between the second and the fifth years relatively few patients with active signs of inherited syphilitic infection are seen, but from then on until puberty many cases are encountered. As stated before, but few of the late cases give a history of previous lesions and the infection seems to have been latent since birth in the majority. The factors which lead to the development of these acute cases in late childhood are unknown. We know that, as a general rule, any infection in childhood lowers a previously acquired immunity or resistance to some other infection, as the lowering of resistance to tuberculosis following measles, and it is probably in something of this nature that the explanation for the development of acute lesions in long-standing quiescent syphilis will be found. Trauma would seem to be a factor in some cases.

It is the growth in the past few years of the number of pathological conditions which have been shown to be the result of "tardy" syphilis that has made the study of inherited syphilis of so much importance and interest. In order to show the protean character the infection assumes in childhood, and how little related are the clinical conditions due to the same infection, I have tabulated the lesions occurring in 100 cases of late syphilis. These are made up of two series of consecutive cases, one of 74 reported one and a half years ago[8] and the last 26 cases admitted to the Children's Hospital.

BONES:	
Periostitis tibia	4
Periostitis skull	1
Osteomyelitis	1
JOINTS:	
Acute arthritis knee	8
Acute arthritis ankle	1
SKIN:	
Macular eruption	1
Condyloma anus	3
Gummata	3
Alopecia	3
EYE:	
Interstitial keratitis	24
Choroiditis	1
ULCERATIONS:	
Nasal	2
Laryngeal	1
Pharyngeal	1

CENTRAL NERVOUS SYSTEM:[9]	
Mental deficiency	23
Cerebrospinal syphilis	14
Hemiplegia	6
Epilepsy	5
Spastic paraplegia	4
Chorea	2
Hydrocephalus	2
MISCELLANEOUS CONDITIONS:	
Ozena	1
Enlarged spleen (only symptom)	1
Torticollis	1
Aortitis	1
Obscure abdominal pain	1
Obscure pain in legs	2
Endarteritis obliterans	1
Paroxysmal hemoglobinuria	1
Raynaud's disease	1
Hutchinson's teeth	4

The thing standing out most prominently in this table is the great preponderance of syphilis of the central nervous system.

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[8] Veeder and Jeans, Late Hereditary Syphilis, Am. Jour. Dis. Child., 1914, viii, 283.

[9] 47 patients showed lesions of the nervous system.

This is contrary to the usual teaching of hereditary syphilis. Holt, for example, in the last edition (1911) of his text-book says of hereditary syphilis, "The different lesions of the central nervous system which may be due to syphilis are all quite rare." In 47, or approximately one-half of our series of 100 "late" cases, the infection appeared in some form of lesion of this system. The other conditions, as periostitis, Hutchinson's teeth, arthritis, interstitial keratitis, etc., which are usually described as the most common, were all present in the series, but in a much smaller percentage.

I have gone over our records to find in what percentage some of these conditions have a syphilitic basis. Hydrocephalus has always been charged against a specific infection to a greater or less degree. Of 13 cases upon which we made Wassermann tests, 3, or about 23 per cent., were positive; 31 cases of epilepsy have been tested, and 6, or 20 per cent., gave positive reactions. Spastic paraplegia is most interesting, as only recently has there been a connection with syphilis suggested. Syphilis was present in 3 of 10 cases, or 30 per cent. in our records. Holt did not happen to meet with a single positive case in eight tested, but Findlay obtained 13 positive tests in a series of 33 cases examined. Hemiplegic children gave the highest percentage of positive reactions, 6 out of 12 cases, or 50 per cent., having syphilis.

A few years ago a French writer, whose name I have forgotten, reported that he had obtained positive reactions in nearly all of a small series of children with chorea. This was not confirmed by subsequent investigations, and it is probable that considerable error in the technic of making tests must have crept in. We have tested nearly 40 cases of chorea and in 2 obtained positive reactions. In 1 of these the chorea apparently had a syphilitic basis, but in the other it might have been a chance association. Neither had any signs of a rheumatic infection. The one case—a maniacal chorea—responded immediately to specific treatment. In order to see if the therapeutic test was of any value we treated several non-specific choreics in the same way without the slightest effect being produced. Comby[10] has recently reported that he found evidence of syphilis in 7 of 39 cases of chorea, but Koplik[11] in a smaller series came to the conclusion that there was no relationship between the two.

Mental deficiency has been a favorite subject of study from the standpoint of syphilis in the last few years, and with the most contradictory results when large groups of institutional defectives have been examined. What, from our view-point, is of more importance than the percentage of mental deficiency due to syphilis is the number of syphilitic children showing mental deficiency.

[10] Etiology of Chorea, Arch. d. Med. d. Enf., 1915, xviii, 517.

[11] Relationship of Syphilis to Chorea of Sydenham, Arch. Pediat., 1915, xxxii, 561.

Thus 23 out of 100, or approximately one-fourth of the "late" group, were defectives. In addition then to the high death rate of inherited syphilis we must add one-quarter of the living children as "worse than dead."

Recently a new test for the presence of protein substances in the spinal fluid has been advanced which it is claimed is of value in the differential diagnosis of cerebrospinal syphilis from other diseases of the *central nervous* system. This is the "colloidal gold" or Lange test, in which various dilutions of the spinal fluid under investigation are added to the reagent in a series of tubes. According to the discoverer of the test each disease produces a color change in certain tubes—or a zone of color change—which is characteristic of the disease. Thus in syphilis the zone of change is in the lower dilutions and in tuberculous meningitis in the higher. As yet the test has been almost exclusively used in the diagnosis of paresis and other parasyphilitic conditions. Dr. Meredith Johnston has been making a general study of the spinal fluid in childhood in our laboratory, and among his cases were 20 of hereditary syphilis. All of these gave a positive Wassermann on the blood. In 15 of the 20 cases the central nervous system was involved. In 14 of these 15 the Lange test was positive while the Wassermann was only positive on the spinal fluids of 8 of 14 tested. Thus only 1 case gave a negative Lange while in 6 the Wassermann was negative. Both the Wassermann and Lange tests were negative on the spinal fluids of all 5 cases without clinical signs of central nervous involvement. The only other disease which Dr. Johnston has found which gives a similar zone of change to that occurring in cerebrospinal syphilis is acute anterior poliomyelitis, and in this the reaction is only transitory and not persistent as it is in syphilis.

WASSERMANN REACTIONS. From what has been said it is obvious that we attach a great deal of importance to the Wassermann reaction. Like all delicate laboratory tests it is only of value when carefully controlled and made by a skilled technician. A poor Wassermann test, or one in which there is a question as to the accuracy of the worker, is worse than none, while a good test is of great value. We look upon a Wassermann reaction as a symptom or an indication of infection rather than of immunity, and in this sense it is comparable with the tuberculin reaction. When a case of syphilis is cured the reaction becomes negative, but the patient again becomes susceptible to infection, and a number of cases have been reported where this has taken place. The longer the infection has been present the more apt is the reaction to be positive, hence the high percentage of positive reactions in tertiary and parasyphilis, and likewise in inherited syphilis. We have seen but one patient with late hereditary syphilis whose blood failed to give a positive reaction, and in this the diagnosis was somewhat questionable. For practical purposes then we can say that in our experience all of the cases of late hereditary syphilis give a positive reaction. This does not hold true for the cases of an infantile type. In the series of 100 cases reported above the blood was tested in 82 with the following result:

Positive	76 or 92.6	per cent.
Doubtful	1 or 1.3	" "
Negative	5 or 6.1	" "

For the two types (over 300 cases) the percentage of positive reactions is about 98. This corresponds with the figures of Boas,[12] who states in his book on the Wassermann reaction that hereditary syphilis gives a higher percentage of positive reactions than the other forms. He tested 53 infants with manifest lues and 54 older children with late lesions and all reacted positively. A number of newborn syphilitic infants reacted negatively, although most of this type of cases gave a positive reaction. A number of writers have called attention to the fact that a small percentage of newborn infants give a negative reaction and later a positive one. This may be explained on the basis that infection occurred just before birth and that some time must elapse before the formation of reactive bodies. Three of the five negatively reacting infantile cases in our series do not belong in this group, as two were three months of age and one five months when tested. All were clinically syphilitic and there was syphilis in the parents of the one child whose parents submitted to tests. Positive reactions in non-syphilitic children are rare, so rare I feel the technic must be faulty. I can recall having seen but one such case, and this reacted negatively on a control test. Lederman found 3 in 650 non-syphilitic infants, and these might have been latent cases. Occasionally a weakly positive transitory reaction has been reported in scarlet fever, pneumonia, influenza, and other infections. We have tested a number of scarlet fever cases as well as other febrile conditions without finding a single positive reaction.

We can say then that positive reactions in non-syphilitic patients are extremely rare, that in all of the patients with the late type and over 90 per cent. with the infantile type of hereditary syphilis the Wassermann reaction is positive. It is understood, of course, that these figures refer to untreated cases.

My personal experience with the luetin test of Noguchi is very limited. It most certainly cannot offer any advantages over the Wassermann reaction insofar as the furnishing of diagnostic information in hereditary syphilis is concerned, and as we have had dependable laboratory workers making tests we have neglected the luetin test. Its simplicity offers great practical advantages.

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[12] Die Wassermansche Reaktion (2d ed., Berlin), 1914, p. 110.

Recent reports have been somewhat more favorable than the early ones, but the opinion is quite general that the Wassermann reaction is the preferable of the two.

TREATMENT. In general we are accustomed to regard hereditary syphilis as a disease particularly amenable to treatment. If we judge the results of the treatment by its immediate effect upon clinical symptoms this holds true, but it is not true when we consider treatment in its relation to the ultimate cure of the disease. Most acute hereditary syphilitic lesions disappear rapidly under specific treatment with the exception of interstitial keratitis, but the chronic lesions of the central nervous system are but little affected. It is extremely difficult to obtain a persistently negative Wassermann reaction as the result of treatment, and particularly so in the "late" cases. We have treated some cases intensively and persistently for over three years without effect. We have obtained negative Wassermann reactions in the infantile cases following intensive treatment, but in surprisingly few cases considering the entire number treated. In these "infantile" cases, as a matter of fact, the outcome of the case, as far as life or death is concerned, depends far more on the condition of the patient's nutrition than upon the character of the specific medication. If a long series of cases are studied it will be found that the therarpeutic results are disappointing as a whole.

We have used various methods of treatment in our cases, including over 100 in which neosalvarsan was used in combination with mercury. It is the drug of choice to make an acute lesion—as a rash or an arthritis for example—disappear in the shortest time, but for the long-continued treatment which is necessary mercury is preferable. The most satisfactory form of mercury for use with children in our experience is gray powder.

REPORT OF A CASE ILLUSTRATING THE ANATOMICAL SEAT OF MOBILE SPASMS.

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AND

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THE following is the history of the case of a child who, from the age of six months to the sixth year when he died, suffered from continual choreic and tonic spasms, involving nearly all the muscles of his body, including the neck and face.

The case has this importance that it shows an anatomical seat of such spasms as those of chronic chorea, of spasmodic tics, and of myotonia.

SUMMARY. A child, aged six years, born prematurely; normal until the fourth month; then an attack of stupor, etc., diagnosed as "meningitis," then development of clonic and tonic movements involving face, throat, neck, trunk, arms, and legs, the legs being mainly rigid, so that the child could only imperfectly stand or walk; no paralyses, no atrophies, no anesthesias, special senses normal, intelligence retarded, but not seriously.

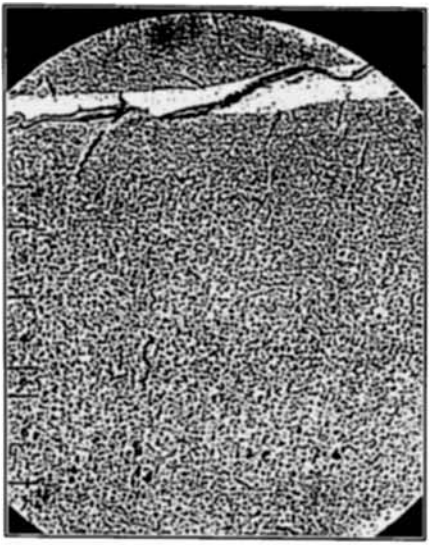

FIG. 1.—Anterior cerebral convolution; arm area × ⅔. Compare Fig. 14. The lines on the side indicate approximately the cortical lamina of this area according to Campbell.

Duration of condition five and one-half years. Death following operation to resect posterior spinal roots.

Autopsy. No gross lesion of brain or cord; brain of normal size and weight.

Microscopically the motor and premotor cortex showed disturbance in lamination of cells, degenerative changes of cells, deficiency in size and number of large pyramidal cells. Changes less marked in posterior central convolution. Changes similar to those of ante-

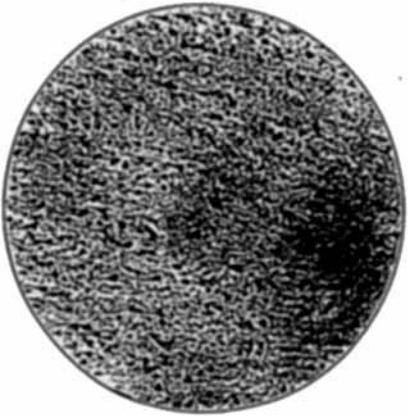

FIG. 2.—Anterior central convolution; arm area × $\frac{1}{150}$, showing fourth, fifth, and sixth layers.

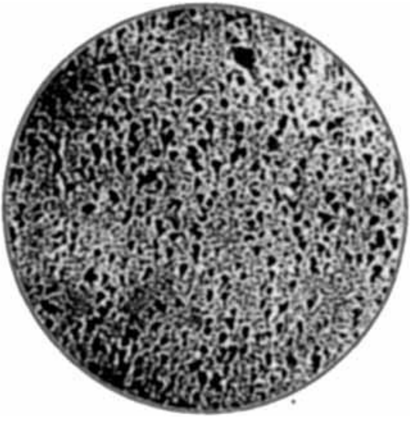

FIG. 3.—Anterior central convolution; arm area × 200.

rior central convolution though much less marked in the thalamic and subthalamic region. Nuclei of columns of Goll and one pyramidal tract show some deficiencies.

The tonic and clonic spasms with some permanent rigidity of the lower extremities were the main features of the case. The tonic spasms caused an apparent spastic paraplegia, although there was no real paralysis, nor objective evidence of involvement of the pyramidal tracts, and both the corticospinal and the peripheral motor neurons showed no or slight signs of degeneration.

History. K. R., male, aged three years and eleven months was brought to me for consultation by Dr. Morissy, of Connecticut. He is the second of three children. The parents are healthy with no history of lues. The boy was born prematurely (six weeks before the time) with a rather long labor, but without any instruments. He had no convulsions, and he grew like a normal child until he was about four months old, when he was taken with what was called "meningitis" and was ill in bed for several weeks. He had a number of convulsions at that time and was in a stuporous condition

After coming out of this he began to develop clonic and tonic spasmodic movements involving the face, tongue, neck, trunk, and extremities; these continued without interruption.

He was first seen by me in April, 1909, when he was three years and eleven months old. He was then fairly well grown but poorly nourished.

His body and extremities, neck and face were in continuous spasmodic movements. The legs were kept mostly in extension, but there was no permanent and absolute contracture and he could at times support himself and with much help could walk a little.

He could not hold up his head, sit up or stand alone, mainly because of the continuous spasms. The head and neck were particularly affected with clonic and tonic spasms of the right accessory which pulled it toward the left as in wry-neck. There were also retrocollic spasms which pulled his head backward; also spasms of the facial muscles and of the tongue, so that he spoke only indistinctly, though he could talk a little. He understood what was said to him, and though somewhat retarded, he seemed to be fairly intelligent. The eye muscles were not involved, the special senses of vision and hearing were normal.

The limbs were well developed and rather muscular, but were in a spastic condition much of the time. The arm movements were jerky and irregular, and he could not easily bring his hand to his mouth or perform any purposeful acts.

The deep reflexes were exaggerated, and there was a doubtful dorsal toe reflex, but no ankle clonus. There was no anesthesia, superficial or deep.

The boy had a normal sized head, but there was a slight bilateral depression in the skull over the motor area on each side. He had a narrow palate and shell ears.

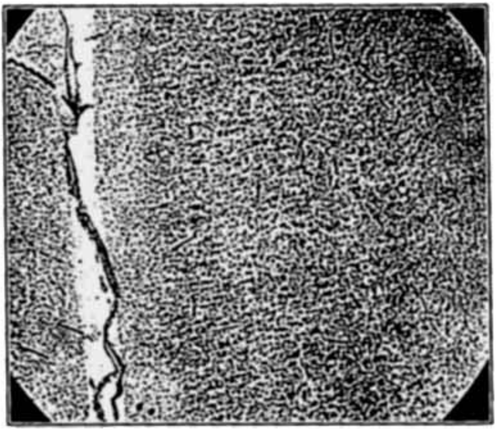

FIG. 4.—Posterior central convolution; arm area × $\frac{2}{3}$.

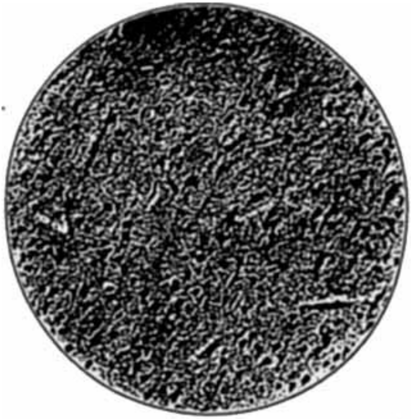

FIG. 5.—Posterior central convolution: arm area × 130.

Three years later the child was brought to me again and sent to the Neurological Institute (December 12, 1912). At that time the following notes were made upon him:

"Child pitifully undeveloped and under nourished. Is seen lying always with the head turned to the right, his arms flexed upon the elbows, his hands clenched, and these tossing and beating about his face and head. The arms can be straightened only with force and then resume their contractured position at once, unresisted.

"The trunk is more quiet than the head or arms and the legs do not move about like the arms, but are held extended partly with the knees slightly flexed. When the child is lifted and his feet brought to the floor he makes no attempt to support himself, and his head is drawn far backward upon the shoulders.

"At the sight of food when hungry the child's movements become greatly increased, the mouth opens widely on the left, the right side hardly sharing in the movement; the hands beat widely about the mouth as though some attempt were being made to assist himself. The feeding of the child is therefore difficult. It is best accomplished by two persons, one to hold him in the sitting position with the back and head supported and his arms clasped in a towel or blanket to prevent them from jerking into his face and mouth spasmodically, and the other person to bring the milk to his mouth in small quantities.

"He cries repeatedly for his mother (a sound similar to 'udda'), and when asked if it is his mother he means, he quickly answers 'ya.' When given a toy rooster in a cage and told what it is, and then later asked to name it, he calls out at once 'oota;' and when he hears an imitation of the crow of a rooster a fleeting smile occurs on the right side of the face alone while during the whole event the arms are moved violently about the ears and face.

"He understood what was said to him and tried to make his wants known."

In addition to the foregoing the following notes were made upon his cranial nerves:

III, IV, VI not involved.

Motor V and sensory V not involved.

Motor VII tonic spasms produced compression of the lips with irregular clonic movements.

VIII normal.

IX, X, XII slightly irregular movements of the tongue, throat, and palate.

XI very violent tonic and clonic spasms of the spinal accessory, the left more than the right.

I to IV spinal nerves: rotators slightly involved.

V to VIII spinal nerves: tonic spasm, adducting arms, flexing forearms, supinating forearms, extending wrists, flexing fingers: The flexing spasms alternate with some extensor spasm and there are also twitching, oscillating and rhythmic movements, causing the head to be twisted and retracted.

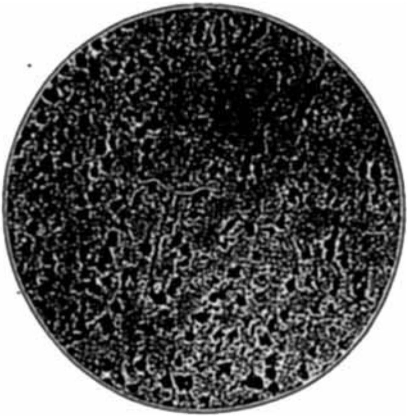

Fig. 6.—Posterior central convolution; arm area × 200.

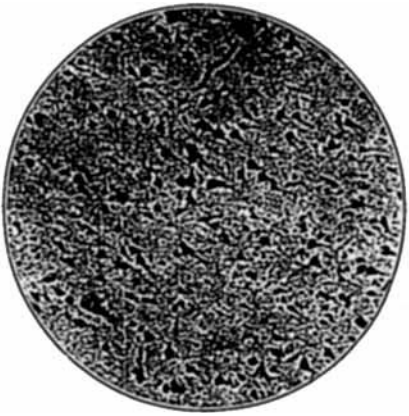

Fig. 7.—Anterior central convolution; leg area × 200.

The most violent movements seemed to be thus involving the neck and arms, and therefore it was thought possible to produce some relief by resecting the posterior roots of this region.

The operation was undertaken with great care by Dr. A. S. Taylor, but the child suddenly stopped breathing and died on the table.

Operation (reported by Dr. A. S. Taylor).

A left unilateral laminectomy was done, involving the 5th, 6th and 7th cervical vertebræ. There was no special difficulty in doing the laminectomy, but there was far more profuse hemorrhage than usual.

The dura was exposed when he suddenly stopped breathing. The heart continued to beat for some time. Artificial breathing was kept up for some time, and saline infusion was given when the heart gave signs of failing, but all to no purpose.

As to the cause of death, the hemorrhage was undoubtedly one factor. The operation had taken only twenty minutes up to that time, so it would not seem fair to hold the anesthetic nor the time consumed in any way responsible.

The unknown factor in the result might be termed lymphatic diathesis, or some of the other names with which ignorance is properly clothed.

Pathological Findings (by Dr. Gere). Examination of the specimen, upon which the clinical and pathological studies of this case rest, showed to the naked eye a brain of apparently normal development in a child of six years, symmetrical in its lateral halves, the convolutions, generally, were deep and full and exhibited no evidences of localized atrophy.

Measurements of the cerebrum, taken after fixation in formalin, may be given as 15 cm. in its anteroposterior diameter, while the greatest transverse diameter measured 11 cm. The weight cannot be accurately given, but, after immersion, one cerebral hemiphere weighed one-half kilo.

The membranes appeared normal except for a mild basilar meningitis, more apparent microscopically than to the naked eye.

The areas inspected include the motor cortex, the postcentral convolution, the thalamic and subthalamic regions, the basal ganglia, red nucleus besides sections through each of the nuclei of the cranial nerves; the spinal cord was also sectioned at different levels.

In observation of the motor cortex attention is directed in a general way to a rather indiscriminate arrangement of cells below the layer of medium-sized pyramidal cells to an apparent diminution in the number of cells of large size, to the difficulty in defining, strictly, cell lamination, and to the distortion of individual cells with, in many instances, an absence of dendritic processes.

Interspersed are to be found many cells preserving their normal pyramidal form and others in varying stages of degeneration.

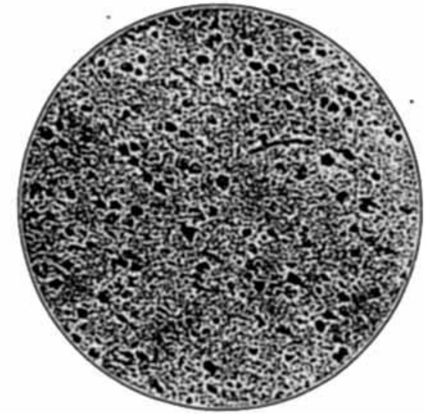

FIG. 8.—Posterior central convolution; leg area × 200.

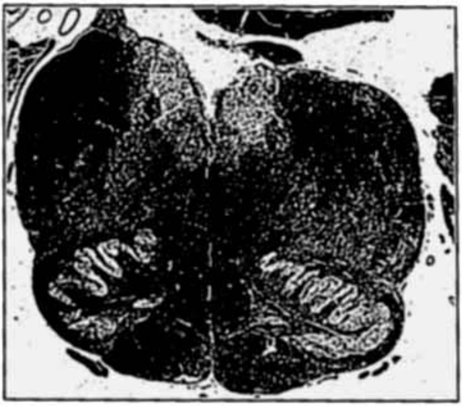

FIG. 9.—Medulla; region of twelfth nerve.

The degenerative process is shown by a tigrolysis varying up to a complete destruction of the chromophylic granules; the nucleus in many of the partly degenerated cells is preserved and placed eccentrically, while the remaining granules are piled up at one pole. A deficiency in size, number, and arrangment of the cells of Betz is very striking.

Inspecting the lamina in order, the plexiform layer does not appear to be disturbed and the cells of the second and third layers are normal except for a few more or less degenerated cells in which the processes are not strongly marked. The layers of large pyramidal cells are not always well defined but appear confused. In the deeper layers of the cortex are many degenerated cells.

In the postcentral convolution cell lamination is far more distinct and the disturbance is present in a slighter degree, though here too, are many degenerated cells lying deep in the cortex.

The thalamic and subthalamic regions and the basil ganglia show nothing remarkable in cell formation and arrangment, and there is no degeneration of cells of the nuclei of the cranial nerves, but the eccentric position of the cell nucleus with the peculiar clumping of the chromophylic granules is, in many cases, pronounced.

Though the clinical history makes note of difficulty in swallowing and of convulsive movements of the face, both the hypoglossal and facial nuclei of each side present no abnormality.

Other nuclei in the region of the hypoglossal, namely, the ninth and tenth, in both the motor and sensory divisions appear entirely normal; nor are changes demonstrable in the sixth, fifth, fourth or third nuclei.

The cells of the anterior horns of the spinal cord from the first cervical segment to the sacral region are normal, but the posterior column nuclei show a few worn cells similar in appearance to those observed in the postcentral and motor areas.

The corticospinal pyramidal system shows no degeneration, but there is a deficiency of medullated fibers in one lateral pyramidal tract throughout the cord. Similarly there is a deficiency without degeneration of the posterior columns, particularly in the columns of Goll in the upper lumbar, the dorsal and cervical regions. In the medulla the arcuate fibers and median lemniscus are well developed and present no pathological changes.

The third and lateral ventricles of the brain are not dilated, and exhibit a thickened subependymal tissue with a tendency to gliosis, though the ependyma itself appears normal, and this is also true of the Sylvian aqueduct, which is very irregular in outline and sacculated.

In the region of the posterior corpora quadrigemina and placed ventral to the aqueduct of Sylvius there appears a formation resembling an obliterated canal by ependyma.

Changes similar and more intense are to be observed in the fourth ventricle, especially in its posterior extremity, where a condition of gliosis undoubtedly exists.

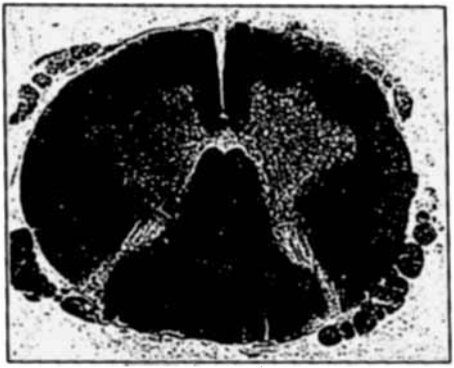

FIG. 10.—Spinal cord, cervical region.

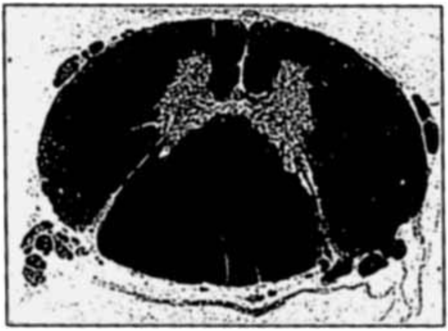

FIG. 11.—Upper dorsal cord.

The choroid plexuses present no particular pathological change. The cerebral vessels are the seat of marked changes which consist of thickened walls, distended perivascular lymph spaces containing many deposits of round cells.

Examination of the cerebellum fails to demonstrate any departure from the normal structure of that organ.

The observations in the above report were confirmed by Dr. James Ewing and Dr. T. H. Ames.

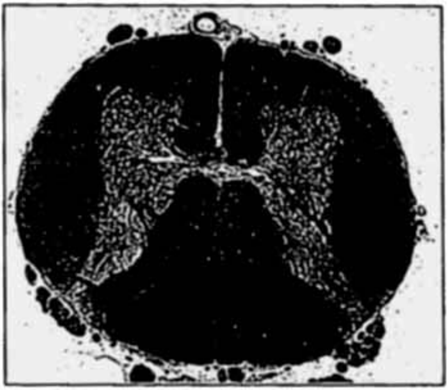

FIG. 12.—Lumbar cord.

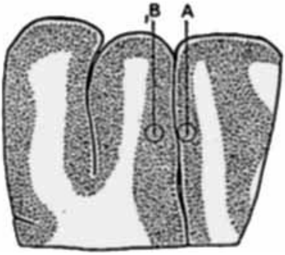

FIG. 13.—Anterior (*B*) and posterior (*A*) central convolutions—arm area—showing location of areas photographed.

The conclusions from this case are that the patient had at the fourth month a low grade infectious polioencephalitis affecting especially the motor cortex and impairing the sensori-motor mechanism, *i. e.*, the dendrites and fibrils. This led not to paralysis but to irregular motor discharges and loss of muscular control. The existence of an abnormally fine pyramidal tract is probably due to some slight involvement of the cells of Betz, and this might perhaps explain spasticity and weakness, but not the various types of mobile spasm seen in the case reported here.

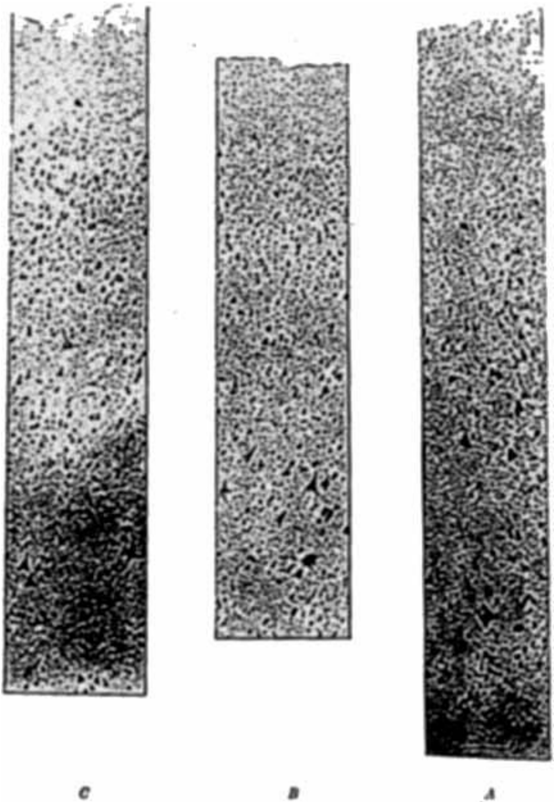

FIG. 14.—*A*, section through the anterior central convolution of a healthy brain; *B* and *C*, sections through the anterior central convolutions of two cases of cerebral spastic hemiplegia with intact pyramidal tracts. One sees in both cases that the deep layers are hardly affected, while the superficial layers are markedly atrophied. (H. Vogt.)

The subject of cerebral hemiplegia and diplegia without involvement of the pyramidal tracts is discussed in full with bibliography by Dr. H. Vogt.[1] In these cases, sometimes at least, the spastic paralysis seems due to atrophy of the superficial layers of the cortex with intact cells of Betz (Fig. 13). In our case it was not so much atrophy of particular layers, but various irregular displacements, degenerations, and focal atrophies. This would explain the irregular motor discharges.

The cortical changes that were found are sufficient to explain the spasmodic symptoms, and as these lesions were induced by some infection four months after birth it is a fair inference that they were primary and not secondary factors in the disease. We believe that they give us an indication of the pathological anatomy of the chronic degenerative myoclonic and myotonic spasms.

It seems to be fairly well established that the chronic, coarse, jerky, ataxic tremors are due to involvement of the cerebellar rubrospinal and extrapyramidal tracts. Such involvement is seen in paralysis agitans, multiple sclerosis, and midbrain and cerebellar disease.

But the clonic and tonic spasms such as are seen in spasmodic tics, torticollis, hereditary chorea, and myoclonias especially are cortical and due to defects and displacements of the cells of the central and precentral convolutions.

This view is supported by the fact that cortical changes are found in chronic and hereditary chorea, in myoclonus epilepsy and in certain localized degenerative tics.

The case presented clinically some of the features of Little's disease, with clonic and tonic spasms, but there was in our case no real paralysis and no involvement of the pyramidal or extrapyramidal tracts, at all adequate to explain the essential features of the symptoms.

A study of the types of cerebral infantile diplegia without anatomical findings has been first and elaborately made by Dr. William G. Spiller.[2]

A full bibliography of this subject is given as stated above by Dr. H. Vogt.

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[1] Lewandow's Handbruch de Neurologie, vol. iii, p. 295.

[2] Jour. Nerv. and Ment. Dis., 1898, p. 81; Univ. Penna. Med. Bull., January, 1905, by Dr. John H. W. Rheim; Amer. Jour. Med. Sc., December, 1909, and later by Berghinz, Revista di Clinica pediatrica, 1903, p. 416.